Remarks/Arguments

The amendments to the specification are made to correct informalities objected to by the Examiner. No new matter has been added by these amendments.

Applicants have furnished a clean copy of Figures 2A and 2B at the request of the Examiner.

In order to further prosecution, Applicants have restricted their claims to those directed to a SF06 protein and/or a nucleic acid encoding an SF06 protein and removed the references to other secreted factor proteins from the claims. Applicants reserve the right to file a divisional application containing these claims at a later time.

Claims 1-11, 19-20, and 43-55 are pending in the present application. Support for the amendments to claim 1 may be found in claim 1 as originally filed as well as in the specification at page 16, lines 24-31. The amendments to claims 2-11 are made to put the claims in proper dependent form. Certain amendments to claims 3, 4, 8, and 11 have been made to correct informalities objected to by the Examiner. New claims 43 and 44 find support in claim 14. New claim 45 finds support in claim 6. New claims 46 and 47 find support in claim 11. New claims 48-50 find support in claim 4. New claim 51 finds support in claim 15. New claims 52-53 find support in claim 16. New claim 54 finds support in the specification at page 26, second paragraph, lines 17-27. New claim 55 finds support in the

specification at page 28, lines 3-14. No new matter has been added by these amendments.

Claims

The Examiner objects to claims 12-22 as being of improper dependent form, since these claims fail to further limit the subject matter of the previous claim. The Examiner argues that claims 12-22 only recite an additional intended use for the pharmaceutical composition of claim 1, and thus do not further limit the subject matter of the claim. Applicants have cancelled claims 12-18 and 21-22, obviating the rejection of these claims. Applicants have also amended claim 1 to recite a method of treating a condition; applicants contend that claims 19 is in proper dependent form because it recites a method further comprising an additional step. Likewise, claim 20 is in proper dependent form as it recites the method of claim 1 further comprising an additional step.

The Examiner objects to claims 4, 7-9, and 11 for certain informalities. The Examiner objects to claim 4 on the ground that it does not end in a period, that it fails to recite proper Markush-type language, that part (c) is grammatically improper, and that the term “99,6%” should read “99.6%.” Applicants have amended claim 4 to correct these informalities.

The Examiner objects to claims 7 on the grounds that the nucleic acid in claim 1 inherently has to be a recombinant nucleic acid molecule since the intended use of the nucleic acid is gene therapy. Likewise, the Examiner objects

to claim 8 on the grounds that since the recited use of the nucleic acid is gene therapy, the nucleic acid must also be a vector. The Examiner further objects to claim 9 on the grounds that a recombinant polypeptide is indistinguishable from a polypeptide. Applicants traverse.

Claim 1 has been amended to claim a method of treating a condition selected from a pancreatic disease, obesity, metabolic syndrome, a metabolic disease, or metabolic dysfunction in a patient in need thereof by administering an effective amount of an agent selected from a polypeptide and nucleic acids encoding this polypeptide. Neither claim 1, claim 7, nor claim 8 recite that the intended use of the nucleic acid is for gene therapy. Nothing in the specification or the claims indicates that the nucleic acids are to be used solely for gene therapy. One skilled in the art, upon reading the claim 1 in conjunction with claims 7 and 8, would recognize that claim 1 encompassed administering any nucleic acid encoding one the listed protein, including, but not limited to, naturally occurring nucleic acids, anti-sense oligonucleotides, primers, hybridization probes, cDNA, mRNA, as well as recombinant nucleic acids and vectors. Claims 7 and 8 thus further limit the invention by reciting that the nucleic acid is either a recombinant nucleic acid (claim 7) or a vector (claim 8).

The Examiner objects to claim 11 on the grounds that the claim recites an improper Markush group. Applicants have amended claim 11 to remove the Markush group from the claim. Applicants have also introduced new claims 51 and 52 to cover the other elements of the Markush group. As such, these amendments obviate this rejection.

35 U.S.C. §112

The Examiner has rejected claim 4 under 35 U.S.C. §112 on the grounds that it is indefinite; the Examiner specifically objects to the recital of a nucleic acid molecule or protein "as shown in Table 2" on the grounds that the database accession numbers in Table 2 are subject to continuous updates and corrections, and thus that the nucleic acid sequence and amino acid sequence of the claimed molecules may change over time. Applicants have amended claim 4 to recite the specific sequence identification numbers of these sequences as listed in the sequence listing.

The Examiner further rejects claim 4 on the grounds that the term "preferably" renders the claim scope unclear. Likewise, the Examiner rejects claim 8 and 16 on the grounds that the phrase "particularly" renders the claim scope indefinite. Applicants have amended the claims to remove these phrases. Claim 16 has been cancelled.

The Examiner has rejected claims 1-22 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner specifically argues that the specification fails to provide support for the genus of functional polypeptide variants and fragments. Applicants have amended claim 1 to recite, instead, proteins having at least 85% identity to a SF06 protein and nucleic acids encoding a protein having at least 85% identity to a SF06 protein. As such, the specification teaches the specific essential structure

of the proteins to be used in the claimed invention, and thus the claimed invention is sufficiently described by the specification.

The Examiner has rejected claims 1-22 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner argues that there is insufficient enabling support in the specification for how to make and use SF06 proteins and functional variants and that one of ordinary skill would be required to engage in undue experimentation in order to make and use functional variants of the SF06 proteins and nucleic acids encoding them in order to achieve a clinically meaningful result. Applicants have amended the claims to recite a method of treating a condition selected from a pancreatic disease, obesity, metabolic syndrome, a metabolic disease, or metabolic dysfunction in a patient in need of such treatment, comprising administering an effective amount of an agent comprising a protein having at least 85% identity to SF06 and/or nucleic acids encoding a protein having at least 85% identity to SF06. Furthermore, applicants note that the specification offers guidance on which amino acids may be substituted for amino acids in the protein sequence (see specification, p. 12, l. 7-15).

Furthermore, as of the filing date of the application, one of ordinary skill in the art would be able to predict with some amount of clarity and without undue experimentation which amino acid substitutions were likely to be successful. Though the Examiner cites several references and asserts that these references show that one of skill in the art cannot predict whether a particular substitution will be effective or not, these references also teach that “proteins are surprisingly

tolerant of amino acid substitutions" (see Bowie et al., p. 1306, 2nd column) and that sequence similarity between protein structures results in proteins with similar tertiary structure (see Id., p. 1308, top of second column) and thus, presumably, with similar function (see Id., p. 1306, first column: "it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome."). As such, the specification would enable one having ordinary skill in the art to make and use a protein having at least 85% identity to SF06 or a nucleic acid encoding a protein having at least 85% identity to SF06 to be used in the claimed method.

Further, the Examiner argues that the claims are not enabled because there are no working examples of the invention as claimed and the specification does not establish the necessary expression of a SF06 therapeutic protein alone or in combination with an SF06 gene therapy vector to achieve a clinically meaningful result on a specific disease. Applicants traverse. First and foremost, an applicant need not present working examples as evidence of enablement. Second, there is no requirement in the statute or in case law that an applicant present evidence showing that his or her claimed invention is "clinically effective." Instead, the standard is whether the specification enables one of ordinary skill in the art to make and use the claimed invention without undue experimentation. In this case, Applicants teach one of ordinary skill in the art how to perform the claimed methods of treatment. Applicants teach dosage forms for the SF06 proteins and nucleic acids encoding those proteins (see p. 24, last paragraph), how to determine an effective dose for the agents (see p. 25, second paragraph),

and proper dosage ranges for the claimed compositions (see p. 26, first paragraph). As for the methods of diagnosis claimed in new claims 52 and 53, applicants teach how to perform such methods on page 26, second paragraph, and on page 28 in the first full paragraph. One of ordinary skill in the art would be able to perform the claimed methods without engaging in undue experimentation.

35 U.S.C. 102

The Examiner rejects claims 1-22 under 35 U.S.C. §102(b) as anticipated by Barnes, WO 99/42576. The Examiner is of the opinion that Barnes discloses Cbln2, which is identical to the human SF06 peptide. The Examiner further argues that Barnes discloses mammalian Cbln2 polypeptides, as well as nucleic acids encoding such polypeptides, and pharmaceutical formulations comprising Cbln2 polypeptides and a nucleic acid encoding Cbln2. The Examiner is further of the opinion that Barnes discloses that the human Cbln2 polypeptide contributes to regulating metabolism.

Applicants have amended the claims to recite a method of treating a condition selected from a pancreatic disease, obesity, metabolic syndrome, a metabolic disease, or metabolic dysfunction in a patient in need of such treatment, comprising administering an effective amount of an agent comprising a SF06 protein and/or a nucleic acid encoding a SF06 protein to the patient. Applicants also claim a method of modulating pancreatic development comprising administering an effective amount of an agent comprising a SF06

protein and/or a nucleic acid encoding a SF06 protein to the patient. Further, applicants claim a method of regenerating pancreatic cells or pancreatic tissues comprising administering an effective amount of an agent comprising a SF06 protein and/or a nucleic acid encoding a SF06 protein to the patient. While the Examiner argues that Barnes discloses that the human Cbln2 polypeptide contributes to regulating metabolism on page 14, lines 25-28, an examination of this section shows that Barnes only discloses "methods of treating abnormal conditions such as… neurological disorders, parkinson's disease, alzheimiers disease, affective disorders including bipolar and unipolar disorders, schizophrenia, olivopontocerebellar atrophy, Shy-Drager syndrome, and other disorders caused by disruption of synapse function…." Applicants respectfully note that none of these conditions are related to metabolism, metabolic syndromes, metabolic diseases, metabolic dysfunction, obesity, or pancreatic diseases. As such, Barnes does not anticipate claims 1-11, 19-20, and 41-53. Furthermore, Barnes does not disclose the methods of diagnosing a condition selected from pancreatic diseases, obesity, metabolic syndrome, or metabolic diseases or metabolic dysfunction claimed in claims 54 and 55.

The Examiner rejects claims 1-22 under 35 U.S.C. § 102(e) as anticipated by Hu et al., U.S. Patent Application Publication 2004/0248156. Hu et al. disclose polypeptides containing C1q regions and polynucleotides encoding C1q domain-containing polypeptides which are useful in compositions for the diagnosis, treatment, or prevention of various disorders, including diseases/disorders related to lipid metabolism, glucose or blood sugar metabolism, obesity, and

diabetes. Hu also does disclose that a cerebellin precursor, Cbln1, contains a C1q domain. (See paragraph [0007]). Hu et al. also disclose that Cbln2, a distinct polypeptide, also has a C1q region. Nevertheless, Hu et al. refers to Cbln2 to show what is presently known in the art about C1q-containing proteins, and Hu et al. exclude Cbln2 from the list of sequences regarded as sequences of the invention (see paragraph [0215]).

Furthermore, Hu et al. do not teach that the precerebellin-like proteins are effective for the treatment or diagnosis of a condition selected from a pancreatic disease, obesity, metabolic syndrome, a metabolic disease, or metabolic dysfunction in a patient in need of such treatment. Even though Hu et al teach that certain proteins are useful for the diagnosis, treatment, or prevention of diseases/disorders related to lipid metabolism, glucose or blood sugar metabolism, obesity, and diabetes, Hu et al. do not teach that the precerebellin proteins, including Cbln2, are effective for the diagnosis, treatment, or prevention of those disorders. Instead, Hu et al. teach that the precerebellin proteins, including Cbln2, fall into a family of proteins which Hu et al. refer to as the CBLN/Gliacolin group. (See paragraph [0110]-[0103]). Hu et al. disclose that these proteins, and structurally similar proteins, are useful as therapeutics and diagnostics in disorders and diseases involving cellular senescence and neurological disorders, including, but not limited to, disorders in motor function. (See paragraph [0131]).

As such, one of ordinary skill in the art would not consider the teachings of Hu et al. to anticipate the present invention. In order to anticipate a claim, a prior

art document must disclose all of the claimed limitations arranged or combined in the same way as recited in the claim. See Net MoneyIn v. VeriSign Inc., 545 F.3d 1359, 1371 (Fed. Cir. 2008). Hu et al. do not disclose that Cbln2 or nucleic acids encoding Cbln2 are useful in diagnosis or treatment of a condition selected from a pancreatic disease, obesity, metabolic syndrome, a metabolic disease, or metabolic dysfunction in a patient in need of such treatment.

In view of the amendments and the remarks, it is submitted that the present application is now in condition for allowance. Reconsideration and allowance of the pending claims are requested. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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